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Fractional calculus models of complex dynamics in biological tissues

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ABSTRACT

Fractional (non-integer order) calculus can provide a concise model for the description of the dynamic events that occur in biological tissues. Such a description is important for gaining an understanding of the underlying multiscale processes that occur when, for example, tissues are electrically stimulated or mechanically stressed. The mathematics of fractional calculus has been applied successfully in physics, chemistry, and materials science to describe dielectrics, electrodes and viscoelastic materials over extended ranges of time and frequency. In heat and mass transfer, for example, the half-order fractional integral is the natural mathematical connection between thermal or material gradients and the diffusion of heat or ions. Since the material properties of tissue arise from the nanoscale and microscale architecture of subcellular, cellular, and extracellular networks, the challenge for the bioengineer is to develop new dynamic models that predict macroscale behavior from microscale observations and measurements. In this paper we describe three areas of bioengineering research (bioelectrodes, biomechanics, bioimaging) where fractional calculus is being applied to build these new mathematical models.

1. Introduction

The complexity of all living systems is expressed in the structure and function of each cell and tissue. Thus, the biological functions of cardiac muscle, articular cartilage and the spinal cord, for example, are embedded in the three-dimensional structure of each tissue's cells, extracellular matrix, and overall anatomical organization. In the heart, tight electrical contacts between cardiac cells ensure that the pacemaker signals are distributed sequentially to the atria and ventricles; in the knee, the multiple layers within hyaline cartilage distribute transient loads by the rapid movement of ions and water; while in the axons of the spinal cord, sensory input and reflexes are expressed via electrical signals – action potentials – that are directed through complex neural networks. The physiologist seeks to understand such complex behavior by gently probing the cell and tissue environment and by developing mathematical models that describe the resulting perturbations (e.g., ECG changes, gait variation, evoked potential latency). These mathematical models are typically constructed using linear differential equations (LDE) and provide a means for predicting the time variation of the experimentally measured fields, forces and flows that regulate biomechanical, neural and hormonal processes [1].

For many physiological systems LDE models are highly successful (e.g., action potential propagation, blood oxygenation and filtration, and feedback control of insulin secretion) and these models provide the basis for our understanding of normal physiological homeostatis, as well as the changes in system dynamics that bring on or are the consequences of disease. Physiological models describe events both at the molecular level (ion transport, gas diffusion, vesicle formation) and at the organ level (blood clearance, oxygen uptake/gram tissue, muscle tension). As a consequence, much current work in biophysics and physiology is directed at interconnecting molecular process with accurate models of organ (brain, heart, and muscle) function by developing new models that span the intermediate levels of structure between the centimeter

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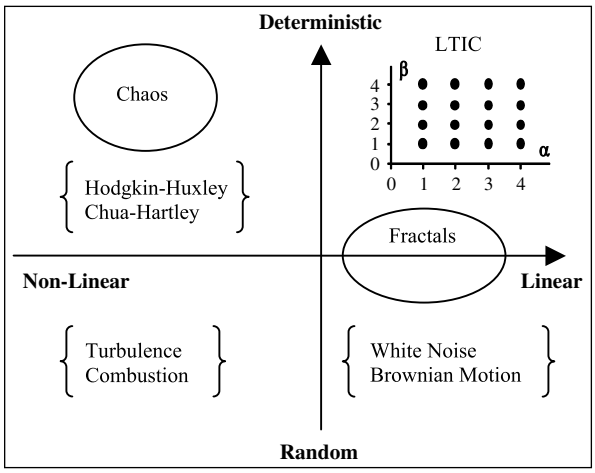

Fig. 1. Illustration of the relationship between the principal kinds of models used for describing complex systems. For conventional linear time-invariant causal (LTIC) models the governing differential equations take on only integer order.

dimensions of gross anatomy and the submicron resolution of histology. In building multiscale models one can try either to employ as much anatomical and histological knowledge as possible – building a highly complex structure with hundreds of components (organelles, membranes, cells, extracellular matrix, etc.) – or to deal empirically with the complexity by defining probabilistic, chaotic or fractal measures (fractal dimensions, Lyapunov exponents, non-Gaussian probability distributions) that capture important features of the observed behavior [2,3]. A diagram illustrating some of the relationships between these approaches is shown in Fig. 1. In this figure the models are characterized on the X-axis by their degree of linearity and on the Y-axis with respect to their deterministic nature. Linear time-invariant causal (LTIC) system models cluster in the first quadrant, while stochastic, probabilistic models fall in the fourth quadrant [4]. In this representation the methods of fractional calculus (linear, deterministic) bundle together in Fig. 1 within the LTIC system models where they interpolate between the integer order differential operators and extend conventional dynamics to fractional order [5]. In practice, it is our belief that such fractional calculus models with differential equations of order α and β can describe more complex biological systems by extending the scales (time and space) over which the models are effective and thus expand the range of phenomena under study [6].

Just as bioinformatics seeks to construct better models connecting gene expression with protein structure and function, bioengineering strives to develop new mathematical tools for describing the complexity of cells and tissues. We might expect that increasing system complexity and connectivity will simply add more nodes and branches to system models and networks. This is the case in molecular dynamics where improved molecular detail provides new information about protein folding and function. But such detailed models are generally intra-molecular and can only predict dynamic behavior for a fraction of a microsecond. Thus, a key bottleneck in modelling complex systems is the trade-off between resolution in space and time. As system complexity grows, we must increase the size of our data arrays and the computational speed of our computers; or alternatively, we must restrict our models to single molecules or to processes occurring on extremely short time scales.

In science and engineering, as in finance, one does not usually get something for nothing. If with increasing complexity conventional LTIC models fail to capture essential details, and if non-linear models exhibit a narrow range of applicability, then what features of fractional order calculus models lead us to believe in their increased relevance to complex systems? First, fractional order models extend our concepts of differentiability and incorporate non-local and system memory effects through fractional order space and time derivatives [7]. These features allow us to model phenomena across multiple time and space scales without having to partition the problem into smaller and smaller compartments. The extent to which a fractional order model will span multiple scales (the nanoscale, microscale, mesoscale, and macroscale) is based on an underlying presumption that fractional derivatives can limn or capture salient features of complex tissue structure. Thus, we overcome the need to define the tissue properties at each level (or unit cell) of our model; they are embedded in an assumed fractal structure. Current work in fractional calculus is directed at answering the questions of where and when such models are valid, but we note that the multiscale patterns observed in muscle fibers (actin, myosin, filaments, fibrils, fibers), tendon (collagen, tropocollagen, fibrils, fibers, fascicles), and nerve fibers (small, medium, large diameter axons) provide a structural rationale for our hypothesis that multiscale structure is effectively encoded in fractional order operations and that the resulting dynamics are expressed through fractional order differential equations.

The extension of linear systems models to include fractional order methods requires learning a new mathematical tool; a tool with which there are substantial issues associated with identifying the appropriate initial conditions and in selecting the proper definition of fractional integration to be used for a given problem [8–11]. Thus, moving to fractional order techniques is not as smooth a transition as that which arises when one moves from an ordinary to a partial derivative, or from a single to

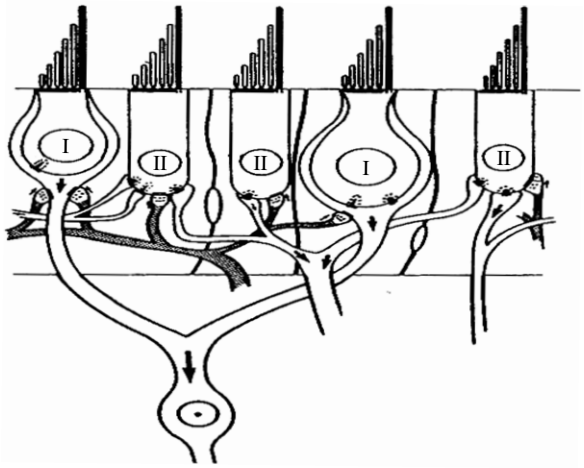

Fig. 2. A drawing of the complex, multiscale neural pathways (hair cells, axons, synapses, neurons) in the vestibular apparatus of the inner ear (adapted from [14]).

a multiple integral. A better metaphor, perhaps, would be the extension of the Riemann integral to the Stieltjes or Lebesgue integral, but even that generalization of integral measure does not quite capture the yin and yang of the relationship between fractional calculus and ordinary calculus. One probably has to go as far as Dirac did in inventing the so-called Dirac delta function (or as Heaviside did in inventing and applying to transient analysis the step function) to appreciate the full range of operations affected.

For example, in conventional calculus the derivative of a unit step function or of a Dirac delta function is not strictly defined; this shortcoming is circumvented in generalized function calculus by defining a generalized — everywhere differentiable — function. In fractional calculus, discontinuous functions such as the unit step and the Dirac delta can be evaluated (as can other discontinuous, even fractal functions), but on the other hand, some of the simple properties of differentiation are lost (e.g., the derivative of the product of two functions). Thus, in applying fractional calculus one must always be on guard to check that the desired mathematical operations – and the sequences of these operations – are allowed.

Despite these restrictions, fractional order models are now being applied to a wide range of problems in bioengineering. In this paper I will first consider a general model of vestibulo-oculomotor system that provides a rationale for fractional dynamics as a distributed relaxation process, and then describe briefly examples from three areas of bioengineering: (i) the electrical impedance of the electrode–tissue interface (a key problem in pacemaker design), (ii) the stress–strain behavior of arterial viscoelasticity and hysteresis (important predictors of heart disease), and (iii) the bulk elastic properties of normal and cancerous breast tissue (malignant and benign). The goal is to illustrate how fractional calculus extends the conventional *R–C* circuit, spring–dashpot, and simple exponential decay models in such a way that the dynamic behavior of the system is more closely tracked over the range of observed physical and physiological variables.

2. Fractional dynamics model

A fractional order model is commonly used to describe the behavior of neural systems [6]. A simple example is the vestibular-oculomotor system modeled by Anastasio [12,13] in the Laplace domain as s^k or s^{-k}, where $0 < k < 1$. The occurrence of s^k behavior in the transfer functions for the neural components of vestibulo-oculomotor systems suggests that its putative role in sensory adaptation reflects a need to control or monitor the underlying biological, physical, or chemical mechanisms. The occurrence of power law transient and dynamic behavior in non-living systems (dielectrics, viscoelastic materials, and electrochemical reactions) implies that the fundamental mechanism is not unique to the anatomical structure or neurological connections of living systems, but most likely reflects diffusion and spatially distributed processes. Thus, the subthreshold behavior of axons, which mimic at their most basic level lossy (RC) transmission lines with fractional impedance relationships, could play a role in understanding synapse complexity, dendritic convergence and generator potential initiation. For example, the convergence of unmyelinated afferent and efferent nerve fibers in the vestibular neuroepithelium has been suggested as an anatomical site where summation of excitatory and inhibitory postsynaptic potentials can occur (see Fig. 2).

In a paper on distributed relaxation processes in sensory adaptation, John Thorson and Marguerite Biederman-Thorson [14] reviewed earlier interpretations for fractional dynamics (non-linear spring, transmission line, and Gaussian distribution of exponential rate constants), which they found, for the most part, to provide an incomplete explanation for the wide dynamic range of sensory adaptations. They subsequently suggested a model based on the weighted summation of exponentials, which as the number of elements increases toward infinity describes fractional order dynamic behavior. This concept has more recently been used by Anastasio [13] to approximate fractional order operators in his analysis of the

vestibulo-ocular system. The basic idea developed by Thorson and Biederman-Thorson is to represent a power law relaxation decay in time (e.g., t^{-k}, where $0 < k < 1$) by a sum of exponentials weighted in an appropriate manner. Starting with the integral definition of the gamma function [6],

$$\Gamma(k) = \int_0^\infty x^{k-1} e^{-x} dx, \quad k > 0, \tag{2.1}$$

if we let $x = ta$, where t is assumed to be a parameter greater than zero, then we can solve for t^{-k} to yield

$$t^{-k} = \frac{1}{\Gamma(k)} \int_0^\infty a^{k-1} e^{-at} da. \tag{2.2}$$

This integral can be interpreted as the Laplace transform of the function $a^{k-1}/\Gamma(k)$. Hence, we see that (2.2) provides a representation for the power law decay as a weighted integral of exponentials. Thus, between the values of a and $a + da$ there exists an exponential e^{-at} with a weight, $a^{k-1}/\Gamma(k)$. Here a has the units of $(s)^{-1}$, and can be viewed as a rate constant. The overall power law relaxation given by (2.2) is the summation of all these contributions for the entire range of possible rate constants. In order to convert this time domain representation into a model for fractional operations we take the Laplace transform of both sides of (2.2). Since

$$L\left\{t^{-k}\right\} = \frac{\Gamma(1-k)}{s^{1-k}}, \quad k < 1, \tag{2.3}$$

and assuming that we can interchange the order of integration for a and t we obtain

$$s^{k-1} = \frac{1}{\Gamma(k)\Gamma(1-k)} \int_0^\infty \frac{a^{k-1}}{s+a} da, \tag{2.4}$$

which is the Stieltjes transform of $a^{k-1}/\Gamma(k)\Gamma(1-k)$. Finally, solving for s^k and if we let $a = 1/\tau$ where τ is the relaxation time corresponding to a particular value of a we obtain

$$s^k = \frac{1}{\Gamma(k)\Gamma(1-k)} \int_0^\infty \tau^{-k} \left(\frac{\tau s}{\tau s + 1}\right) \frac{d\tau}{\tau}. \tag{2.5}$$

Thus, in this interpretation, we see that the fractional derivative operator is represented as an integral or summation of Laplace domain terms each of which correspond to a high-pass filter, and by a similar derivation the fractional integral operator is expressed in terms of an integral of low-pass filters [6]. This is a unifying hypothesis for interpreting the meaning of a fractional order operator because it extends in a natural way the usual progression of modeling linear systems as a series of exponentials. In general, as the complexity of a model increases, typically we increase the degree of the integer order transfer function. Fractional order transfer functions capture some of this complexity in their very definition so fewer individual elements of each subsystem have to be assumed and approximated.

3. Bioengineering applications

Distributed relaxation processes appear to be common in cells and tissues. Therefore, it should not be surprising to see that fractional calculus can play an important role in describing the input–output behavior of biological systems. The physical foundations for this behavior may be sought in the fractal or porous structure of the system components or in the physical characteristics of its surfaces and interfaces. Much work [7] is ongoing to develop a direct link between fractal models of molecules, surfaces, and materials and the fractional kinetics or dynamics of the resulting behavior (polymerization electrochemical reactions, viscoelastic relaxation).

A major attribute of fractional dynamic models is that they interpolate between the known integer order behavior by extending the transfer function models from rational algebraic functions of the Laplace transform parameter s to irrational functions $f(s)$ involving fractional powers of s. This is a natural approach that extends the traditional Laplace transform methods of linear systems analysis [6]. Thus, the fractional dynamics hypothesis is accessible to the engineer and scientist through both Laplace and Fourier techniques (for $s = j\omega$ where j is the square root of minus one and ω is the angular frequency in radians/s). In the following we consider three examples that illustrate aspects of this approach.

Fractional order circuit elements, such as, the impedance: $Z = Z_0/(s)^\alpha$ or $Z = Z_0/(j\omega)^\alpha$, where $0 < \alpha < 1$, have long been recognized as providing a useful model for the transient and the sinusoidal steady state frequency response of dielectrics, biological tissues and bioelectrodes — for a review see the work of Magin and Ovadia [15,6], and a recent book Grimnes and Martinsen [16]. Fractional order circuit elements can be used to develop an electrical circuit model of complex processes, such as, the electrode–cardiac tissue interface of a pacemaker electrode (Fig. 3). A lumped element circuit model for the cardiac tissue/electrode interface is given in Fig. 4. Such models are essential for designing cardiac pacemakers, which must continuously monitor the electrical activity of the heart, and when needed, deliver missing or delayed signals. Fractional calculus appears in the model through the fractional order (or constant phase, $Z = Z_0\omega^\alpha e^{j \arctan(\pi\alpha/2)}$) circuit element Z_D that governs diffusion limited electrochemical reactions at the surface of the electrode.

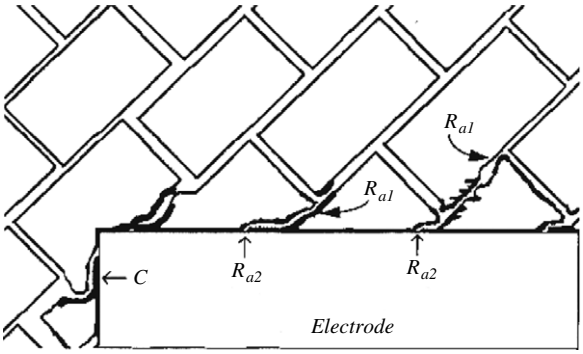

Fig. 3. A drawing of the tissue–electrode interface between cardiac muscle cells and an implanted electrode (redrawn from [15]).

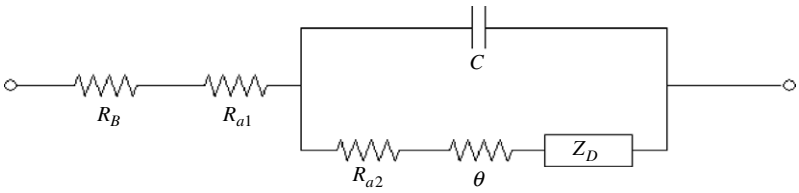

Fig. 4. Tissue–electrode circuit model. R_B is the bulk tissue resistance, R_{a1} and R_{a2} are electrode access resistances, θ is the charge transfer resistance, C is the dipole layer capacitance and Z_D is the fractional Warburg impedance.

If we assume that C, the dipole layer capacitance, is small enough that its reactance can be neglected in comparison with Z_D, then the tissue–electrode equivalent circuit reduces to a resistor in series with Z_D, which can be approximated by two constant phase elements in series. Thus, in the Laplace domain, the overall impedance can be written as

$$z(s) = \frac{v(s)}{i(s)} = R + \frac{1}{s^\alpha C_\alpha} + \frac{1}{s^\beta C_\beta}. \tag{3.1}$$

The corresponding impedance plane plot for (3.1) is shown in Fig. 5 for the simple case of $\alpha = 1/2$ and $\beta = 1$. Such plots match the data measured in experimental studies by Ovadia and Zavitz, [17]. The transient voltage response of this circuit to a step in applied current, such as the leading edge of a pacemaker pulse, is described in the time domain by

$$V(t) = I_0 R + \frac{I_0 t^\alpha}{C_\alpha \Gamma(1+\alpha)} + \frac{I_0 t^\beta}{C_\beta \Gamma(1+\beta)}, \tag{3.2}$$

which gives a power law response that corresponds to that observed in heart stimulation experiments [18].

Thus, we observe that the basic cardiac tissue electrode impedance can be represented by a series combination of a resistor and two fractional lumped circuit elements. The overall transfer function for this model corresponds to the following fractional differential equation:

$$C_\alpha \frac{\mathrm{d}^\alpha V(t)}{\mathrm{d}t^\alpha} = RC_\alpha \frac{\mathrm{d}^\alpha I(t)}{\mathrm{d}t^\alpha} + I(t) + \frac{C_\alpha}{C_\beta} \frac{\mathrm{d}^{\alpha-\beta} I(t)}{\mathrm{d}t^{\alpha-\beta}}, \tag{3.3}$$

if we assume $\alpha > \beta$ and set all initial conditions to zero.

We can use the correspondence between RC electric circuits and viscoelastic networks of springs and dashpots to construct similar fractional order dynamic models for the biomechanical properties of tissues [19]. For example, [20] have modelled the elastic properties of the aorta, *in vivo* in a Merino sheep, using a fractional order generalization of the relationship between stress $\sigma(t)$ and strain $\varepsilon(t)$. Their generalized Voigt model consists of a spring in parallel with two "springpots" of fractional order α and β. The governing fractional order differential equation is

$$\sigma(t) = E_0 \varepsilon(t) + \eta_1 \frac{\mathrm{d}^\alpha \varepsilon(t)}{\mathrm{d}t^\alpha} + \eta_2 \frac{\mathrm{d}^\beta \varepsilon(t)}{\mathrm{d}t^\beta}, \tag{3.4}$$

where E_0 is the elastic constant for a spring, and η_1 and η_2 represent the viscosities of two springpots in parallel with the spring. From this equation the complex modulus $E^*(\omega)$ can be defined for sinusoidal signals as the ratio of stress to strain by

$$E^*(\omega) = \frac{\sigma(\omega)}{\varepsilon(\omega)} = E_0 + \eta_1 (j\omega)^\alpha + \eta_2 (j\omega)^\beta. \tag{3.5}$$

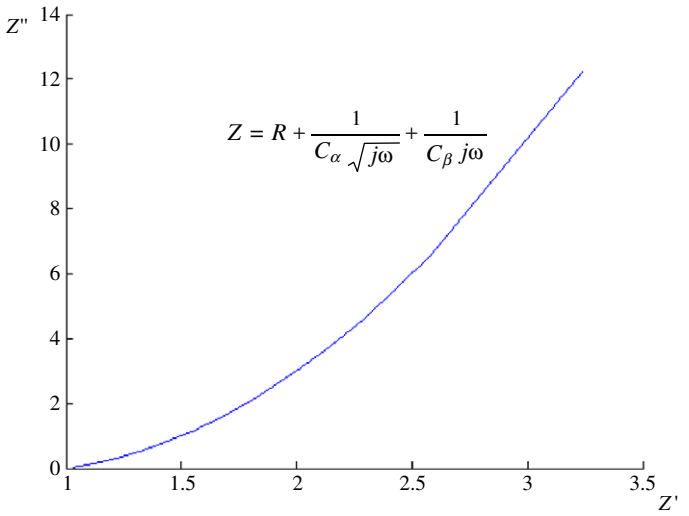

Fig. 5. Impedance plane plot for two constant phase element impedances in series with a resistor. In this example, we set $R = C_\alpha = C_\beta = 1$, and $\alpha = 1/2$, $\beta = 1$ (redrawn from [17]).

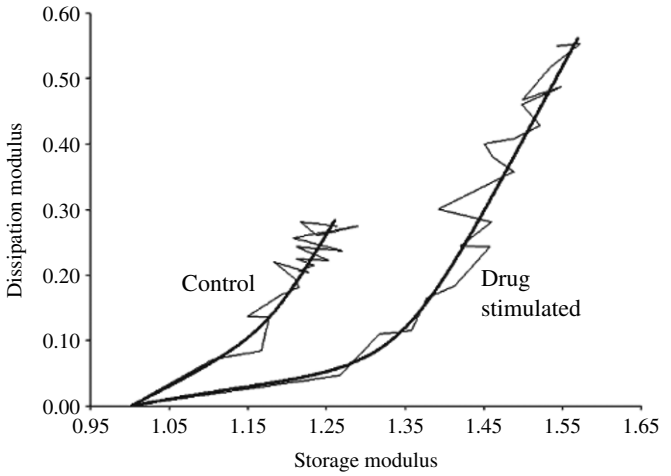

Fig. 6. Vector diagram (complex plane plot) of (3.5) for *in vivo* modulus data from an aorta under control conditions and following application of a vasoconstrictive agent phenylephrine (redrawn from, [21]). In this figure, for the control data we have used $E_0 = 393$ kPa, $\alpha = 0.20$, $\eta_1 = 32.6$ kPa s^α, $\beta = 0.84$, and $\eta_2 = 1.07$ kPa s^β; and for the muscle activation with phenylephrine we have used $E_0 = 411$ kPa, $\alpha = 0.11$, $\eta_1 = 82.2$ kPa s^α, $\beta = 0.80$, and $\eta_2 = 2.73$ kPa s^β.

The real part of $E^*(\omega)$ is defined as the storage modulus and the imaginary part of $E^*(\omega)$ is the loss or dissipation modulus. The storage modulus characterizes the elastic property of the arterial wall while the loss modulus describes the tissue's ability to absorb energy. Both properties change with frequency and govern the pulsatile oscillations of the vessel walls that help to maintain blood pressure in health and disease. This model was found by Craiem and Armentano to give a better fit to *in vivo* data recorded from 2 to 30 Hz than a Voigt model (single spring in parallel with a dashpot) or a fractional Voigt (single spring in parallel with single springpot). A vector plot in the complex plane of the complex modulus for this study is shown in Fig. 6.

In particular, the model (3.5) captures the changes that arise in vessel wall elasticity when a vascular constriction is induced by the local administration of phenylephrine. The authors conclude that the α springpot appears to describe the stretching of the elastic fibers of the aorta (α is close to zero), while the β springpot seems to represent a structural viscous behavior (β closer to 1). As expected the elastic contribution increases – α decreases from 0.20 to 0.11 – following administration of phenylephrine, while the loss term is relatively unchanged (0.84 to 0.80). Thus, for a complex multiscale tissue such as the arterial wall, the fractional order model is able to characterize the important features of its dynamic behavior. This research group has also applied this model to describe the viscoelastic properties of an arterial specimen from humans [21]. In addition, a very similar fractional order Voigt model was recently shown to fit the elastic modulus and creep response data recorded from the membrane of a single red blood cell membrane [22].

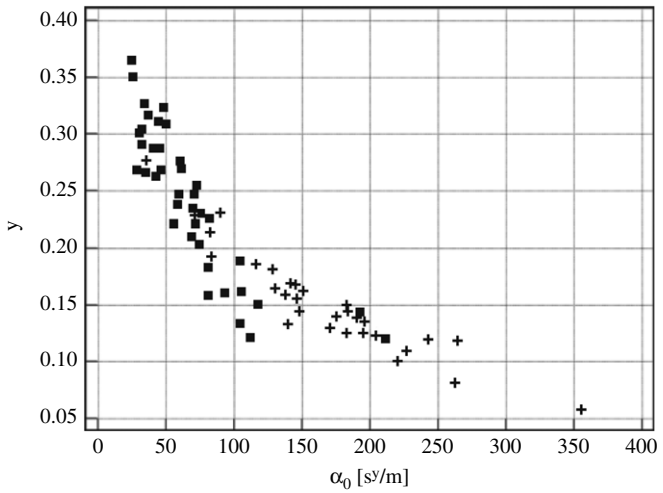

Fig. 7. Plot of benign (+) and malignant (■) breast tumor MRE data for 39 patients. These data are replotted from [23].

Fractional order models have also been used by [23] to fit magnetic resonance elastography (MRE) data for breast tumors. In this technique, MRI is used to image low frequency (50–1500 Hz) shear wave oscillations in the breast. The wavelength and attenuation of the vibrations directly reflect the elastic shear modulus and the viscosity of the tissue through the complex wave vector: $k(\omega) = \beta(\omega) + j\alpha(\omega)$. In MRE these tissue properties are mapped into an elastogram image through an assumed model of the tissue's mechanical properties — usually a purely elastic spring with zero loss, or a Voigt spring/dashpot model. In his study, Sinkus assumed a power law increase in attenuation with excitation frequency, $\alpha(\omega) = \alpha_0\omega^y$ (where $0 < y < 1$), and invoked causality via the Hilbert transform to obtain the propagation constant as $\beta(\omega) = \tan(\pi y/2)\alpha_0\omega^y$. Thus, $k(\omega)$ can be written as

$$k(\omega) = \alpha_0\omega^y e^{-j\pi/2}\sqrt{1 + (\tan(\pi y/2))^2}. \tag{3.6}$$

We know that $k(\omega)$ is related to the complex shear modulus $G^*(\omega)$ through

$$k(\omega) = \omega\sqrt{\rho/G^*(\omega)}, \quad \text{and} \quad G^*(\omega) = \left|G^*(\omega)\right| e^{j\theta}, \tag{3.7}$$

so the modulus and phase can be written, where $\gamma = 2 - 2y$, as

$$\left|G^*(\omega)\right| = \rho\omega^\gamma/\alpha_0^2\left(1 + \chi^2\right), \quad \text{and} \quad \theta = \tan^{-1}(G_l/G_d) = \pi y \quad \chi = \tan(\pi y/2). \tag{3.8}$$

The advantage of this model is that it does not specify a particular Maxwell, Voigt, or Kelvin rheological model, but simply assumes an underlying fractional order dynamics, ω^y, and then estimates the fractional power law parameters y and α_0 from the MRE data. Sinkus first verifies this model for a tissue mimicking breast phantom at a fixed frequency of 65 Hz, and then applies the model to human breast tissue by measuring the dynamic modulus at 65, 75, 85, and 100 Hz. A complex plane plot of G_d and G_l gives a straight line with a y value of approximately 0.13 for normal tissue. Analysis of 39 malignant and 29 benign tumors using this method gives a clear separation of the tumors from the normal (and fibrotic) breast tissue, and furthermore separates the malignant from the benign tumors when individual cases are plotted in a graph (Fig. 7) of y versus α_0 (an increase in specificity of about 20% at 100% sensitivity). In earlier studies this group was not able to classify breast tumors on the basis of G_d and G_l alone, so this model provides a significant improvement in cancer detection.

In the three examples considered here, fractional order models were found to provide better fits to electrical and mechanical measurements made on living tissue. Such studies need replication, but these findings provide useful examples of cases where an extension of the "standard" integer order dynamic models of circuits and mechanical systems is warranted. Also, the careful work of Heymans [24] on the dynamic measurement of viscoelasticity in polymers and other so-called "long-memory" materials demonstrates how to derive fractional order material properties from experimental data. Fractional order dynamic models of complex, multiscale systems account for anomalous dynamic behavior in most cases through a simple extension of the order of the operations from integer to fractional. Perhaps, in the future, the development of integrated space and time domain fractional order models will become a more standard component of linear systems analysis, at least as it is applied to living systems. A recent model by Bates [25] shows how power law stress adaptation in lung tissue can be explained through a sequential recruitment model of parallel Maxwell elements (each simply a spring in series with a dashpot). Such models naturally include the history or memory of past states embedded in the dynamics. Clearly, when the structure in living systems is fractal, or when the measured signals exhibit anomalous properties, one should suspect that the dynamics might best be expressed by fractional order models. Much remains to be done in the future, and we look to the philosopher Henri Bergson to provide inspiration, for, as Bergson [26] noted in his 1911 work *Creative Evolution*, "Whenever anything lives, there is, open somewhere, a register in which time is being inscribed".

4. Conclusions

Fractional calculus models provide a relatively simple way to describe the physical and electrical properties of complex, heterogeneous, and composite biomaterials. There is a multiscale generalization inherent in the definition of the fractional derivative that accurately represents interactions occurring over a wide range of space or time. Thus, we can avoid excessive segmentation or compartmentalization of tissues into subsystems or subunits — a system reduction that often creates more computational and compositional complexity than can be experimentally evaluated. Finally, fractional calculus models suggest new experiments and measurements that can shed light on the meaning of biological system structure and dynamics. Thus, by applying fractional calculus to model the behavior of cells and tissues, we can begin to unravel the inherent complexity of individual molecules and membranes in a way that leads to an improved understanding of the overall biological function and behavior of living systems.

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